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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,055	10/30/2000	Aziz Asghar	1103326-0590	3456

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White & Case
Patent Department
1155 Avenue of the Americas
New York, NY 10036-2787

EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 05/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,055	ASGHAR ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the response filed 2/21/06, claims 9-13 have been cancelled, and claims 14, 17-19 amended. Claims 14-19 remain pending.

Claims 14-19 are examined in this Office action.

Applicants' arguments filed 2/21/06 have been considered and found persuasive in part. The rejection of claims 9 and 13 over Alam S. (*Canadian Journal of Anaesthesia,* 1996) in view of Martin *Neuropharmacology,* 1985) is withdrawn.

The abbreviation **IBS** is used hereinbelow to denote "irritable bowel syndrome".

✧

Claims 14-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,221,887. Although the conflicting claims are not identical, they are not patentably distinct from each other. USP '887 discloses methods of using compounds to treat inflammatory disorders. Among the preferred compounds (col 2, line 60) is remacemide. Among the disorders to be treated are the following (col 2, line 45+):

> conditions of the GI tract including aphthous ulcers, Crohn's disease, atrophic gastritis, gastritis varialoforme, ulcerative colitis, coeliac disease, regional ileitis, peptic ulceration, pyresis, pain and other damage to the GI tract, for example damage from infections by, for example, Helicobacter pylori, or treatments with non-steroidal anti-inflammatory drugs.

One of ordinary skill would conclude that if the symptoms of all the foregoing diseases can be alleviated, then at least one of the symptoms of IBS can be

alleviated. Further, one of ordinary skill would conclude that if the symptoms of all the foregoing diseases can be alleviated, then the visceromotor response to colorectal distension will be attenuated.

Thus, the claims are rendered obvious.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-19 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have shown that compounds falling within the scope of formula I are effective to reduce the visceromotor response to colorectal distension. However, applicants have made no attempt to relate this finding to the claimed invention. The claimed invention is treatment of IBS. Applicants have not shown that colorectal distension invariably accompanies IBS, or that it usually accompanies IBS. And even if it is true that colorectal distension invariably accompanies IBS, there is no evidence of record that reducing the magnitude of the visceromotor response to colorectal distension in any way provides therapeutic relief to patients suffering from IBS. Applicants have made no assertion (or

provided any evidence) that the underlying inflammation is affected one way or another by the compounds.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. There is no evidence that the skilled gastroenterologist would believe that colorectal distension qualifies as a suitable model for IBS, or that attenuating the visceromotor response to colorectal distension provides any sort of benefit to the patient suffering from IBS. There are no "working examples" which show benefit to the mammal stricken with IBS.

In response to the foregoing, applicants have attributed to the examiner the assertion that inflammatory bowel disease is equivalent in all respects to inflammatory bowel syndrome. The examiner has made no such assertion. With regard to the principal matter at hand, applicants have argued that the following web address provides evidence to support the proposition that if a compound is effective to reduce the visceromotor response to colorectal distension, the compound will be effective to treat IBS:

http://www.ccfa.org/about/news/ibsoribd

At this location, the following passage is present:

> "Symptoms can vary widely among individuals, but most IBS sufferers experience some degree of chronic and persistent abdominal pain, constipation, diarrhea, or constipation alternating with diarrhea.
>
> Other symptoms include increased amounts of mucus in the stool, gassiness, abdominal bloating (the sensation of fullness), **abdominal distention (swelling)**, an urge to move the bowels with the inability to do so, and occasionally, nausea. Symptoms commonly occur after eating a large meal or when you are under stress. Often, symptoms are temporarily relieved by having a bowel movement."

Applicants have seized upon the mention of "abdominal distention" as the basis for their conclusion. Applicants have argued that because abdominal distention is one of the symptoms of IBS (irritable bowel syndrome), and because the compounds (to which the claims are directed) are effective to reduce the visceromotor response to colorectal distension, it follows that the compounds will be effective to provide perceptible relief of clinical symptoms of the disorder. However, there is no basis for this, and there is no recognition in the prior art that this might be true. Further, applicants have declined to speculate as to which of the various symptoms of IBS might be mitigated, and there is no logical basis for assuming that even one of the symptoms will be mitigated. Applicants have not actually shown a relationship between abdominal distention and visceromotor response thereto, but even if there is, the mere fact that this visceromotor response can be attenuated does not mean that any sort of therapeutic efficacy will be realized. Furthermore, if the only "symptom" that is mitigated is that of pain perception, then applicants do not have a treatment of the disorder *per*

se, but rather of the pain that accompanies it. In any case, applicants have not established that any of the symptoms of IBS can be alleviated, and accordingly "undue experimentation" would be required to practice the claimed invention.

✧

Claim 14 is objected to. In formula 1, the "2" in the "CH2" group should be present as a subscript, i.e., the following: $-CH_2-$

✧

Claims 14-19 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The claims are indefinite as to the manifestations of a successful treatment. Normally the term "treatment" means that the symptoms of a disease are mitigated so that the patient "feels better" to at least a perceptible degree. Thus, in general a claim drawn to a method of treating irritable bowel syndrome would mean that inflammation of the gut is perceptibly mitigated. Not so in the instant case. Applicants have chosen a rather arcane measure of success, and one which affects neither the inflammation itself nor the well being of the patient. As they stand, the claims encompass the possibility of reducing the inflammation with which the patient is suffering. This particular rejection asserts indefiniteness, rather than lack of enablement, but the foregoing explanation is provided because it is relevant. In any case, as indicated, the claims are indefinite as to the manifestations of a successful treatment. Perhaps one option would be the following:

  A method of treating irritable bowel syndrome comprising administering a patient in need thereof a compound of formula I for a time and under conditions effective to attenuate the visceromotor response to colorectal distension.

In response to the foregoing, applicants have made arguments as to what one of skill would not expect to see in a successful treatment, but applicants have declined to even speculate as to what one might see if the treatment were successful. If applicants cannot recognize a successful treatment when it occurs, then how would the skilled artisan be able to...? Applicants have also argued that other examiners have abstained from imposing this ground of rejection. However, that in and of itself does not make this rejection improper. Furthermore, in most other cases, the applicants are willing to at least hazard a guess as to how they would recognize the outcome of a successful treatment. In the instant case, applicants are not even willing to do that, and so it is very unclear as to what "success" means, particularly since the compounds are ineffective to alter the course of the inflammatory process.

- Claim 16 is not properly dependent on claim 14. Applicants are requested to explain why it is that they believe this compound falls within the scope of the genus of formula I.

✧

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the

inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 14 is rejected under 35 U.S.C. §103 as being unpatentable over Schneider (USP 6,048,543).

Schneider discloses (e.g., col 19, line 10) that glycine can be used to treat inflammatory bowel diseases.

Applicants have argued that inflammatory bowel disease is completely unrelated to inflammatory bowel syndrome. While it is true that these two disorders are not the same in all respects, there is overlap of the symptoms. The gastroenterologist of ordinary skill would expect that if a compound is effective to significantly mitigate the symptoms of inflammatory bowel disease, it will be effective to achieve at least some perceptible effect in the treatment of IBS.

The rejection is maintained.

✧

The reference cited on the IDS filed 2/21/06 has been stricken. The web address should be specified, presumably the following:

http://www.ccfa.org/about/news/ibsoribd

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at (571)272-0974. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON, PH.D.
PRIMARY EXAMINER